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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/801,346	03/06/2001	Vladimir L. Makarov	UMIC:039USC1	7290

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EXAMINER

KIM, YOUNG J

ART UNIT	PAPER NUMBER
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1637

15

DATE MAILED: 04/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/801,346

Applicant(s)

MAKAROV ET AL.

Examiner

Young J. Kim

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 105-135 is/are pending in the application.
- 4a) Of the above claim(s) 107-111 and 116-122 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 105,106 and 123-135 is/are rejected.
- 7) ☒ Claim(s) 112-115 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_.
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5. 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Election/Restrictions***

Applicant's election without traverse of species ii) Chemical fragmentation of DNA sample, drawn to claims 112-115, in Paper No. 14 is acknowledged. The generic claims embracing this elected species will be examined together, resulting in examination of claims 105, 106, 112-115, and 123-135.

Claims 107-111 and 116-122 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 14.

### ***Priority***

This application, in its chain of priorities, rely on U.S. Application Serial Number 08/811,804, which has a filing date of March 6, 1997. Upon perusal of the application, the specification of the '804 application does not contain support for the claimed subject matter in the instant application, and therefore, the priority to the '804 application is denied absent evidence to the contrary.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claims 123-125 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 123-125 recites that the DNA fragments that lack 3' hydroxyl are *conditioned* through the use of a 3' exonuclease with some embodiments drawn to various enzymes that have 5' to 3' exonuclease activities.

Claims 123-125 depend from claim 105 which requires that the *conditioning* of the DNA fragments through the step of treating the fragments with an exonuclease *incorporates a 3' hydroxyl group thereon* (sub-step (b)). However, it appears that the exonuclease cuts the fragments to *produce* a hydroxyl group and not *incorporate a 3' hydroxyl group thereon* (or on the 3' end of the DNA fragment). Therefore, it is confusing how treating the DNA fragments with an exonuclease would *incorporate* a 3' hydroxyl group to the 3' end of the fragments without first cutting the fragments.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

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Claims 105, 106, 123, 126, and 127 are rejected under 35 U.S.C. 102(e) as being anticipated by Legrain et al. (U.S. Patent No. 6,531,284 B1, issued March 11, 2003, priority February 18, 1998).

Claims are drawn to a method of preparing a DNA molecule, the method comprising the steps of obtaining a sample DNA wherein the sample includes DNA fragments that do not have a 3' hydroxyl group and conditioning the DNA fragment of the sample that lack a 3' hydroxyl by incorporating a 3' hydroxyl group thereon.

Legrain et al. disclose a method of preparing a DNA molecule, wherein the method comprises sonicating a DNA sample (or fragmenting, limitation of claim 106), producing some DNA fragments which do not have 3' hydroxyl group, followed by their treatment with Mung bean nuclease which produces a blunt end with 3' hydroxyl group (therefore, *conditioning* the fragments to incorporate 3' hydroxyl group) (limitation of claims 105 and 123, column 30, lines 40-43).

The *conditioned* DNA fragments are exposed to double stranded adaptors (limitations of claims 126 and 127, column 30, lines 45-54).

Therefore, Legrain et al. anticipates the invention as claimed.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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Claims 124, 125, and 128-135 are rejected under 35 U.S.C. 103(a) as being unpatentable over (U.S. Patent No. 6,531,284 B1, issued March 11, 2003, priority February 18, 1998) in view of ~~A Legrain et al.~~ Willems (Biotechniques, January 1998, vol. 24, no. 1, pages 26 and 28).

Legrain et al. disclose a method of preparing a DNA molecule, wherein the method comprises sonicating a DNA sample (or fragmenting, limitation of claim 106), producing some DNA fragments which do not have 3' hydroxyl group, followed by their treatment with Mung bean nuclease which produces a blunt end with 3' hydroxyl group (therefore, *conditioning* the fragments to incorporate 3' hydroxyl group) (limitation of claims 105 and 123, column 30, lines 40-43).

The *conditioned* DNA fragments are exposed to double stranded adaptors (limitations of claims 126 and 127, column 30, lines 45-54).

Legrain et al. do not disclose the use of an exonuclease III or a DNA polymerase having a 3' to 5' exonuclease activity.

Legrain et al. do not disclose the use of double stranded adaptors for the purpose of amplification.

Willems discloses a method of amplifying unknown DNA fragments by fragmenting DNAs with an exonuclease III followed by their (fragments) ligation to a double stranded adaptors (pages 26 and 28). The primers which are complementary to the adaptors are utilized in the following amplification step (page 28, 2<sup>nd</sup> column).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Legrain et al. and Willems to arrive at the invention as claimed for the below reasons.

Although Willems do not involve the method of sonication in producing DNA fragments lacking 3' hydroxyl groups, one of ordinary skill in the art would have been motivated to combine this aspect of the teaching from the disclosure of Legrain et al., because the artisans state that:

“[s]onication of the source genomic DNA[,] ensure[s] a random cleavage of the starting DNA material and thus an [*sic, a*] excellent representation of all possible inserts...” (column 10, lines 48-51).

Legrain et al., after the sonication step (which ensures complete random generation of all possible DNA fragments), treats the resulting fragments with a nuclease to produce a 3' hydroxy group to which adaptors could be ligated. Such step would have been easily incorporated into the method of Willems for the purpose of amplifying unknown DNA fragments, since the exonuclease employed by Willems would have produced the same 3' hydroxyl group to the sonicated DNA fragments. The use of adaptors is well known in the art for their advantage of providing a known starting point for nucleic acid sequences comprising unknown sequences (page 26, 3<sup>rd</sup> column, Willem). Therefore, one of ordinary skill in the art would have been motivated to combine the teachings of Legrain et al., that is, sonication of DNA sample, to ensure all possible DNA fragments, with the adaptor mediated amplification of unknown DNAs of Willems, with a reasonable expectation of success.

### ***Conclusion***

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Claims 112-115 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitation of the base claim and any intervening claims.

The prior art neither teaches or reasonably suggests a method of preparing a DNA molecule which employs chemical fragmentation to produce DNA fragments which lack 3' hydroxyl group.

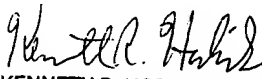
### *Inquiries*

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (703) 308-9348. The Examiner can normally be reached from 8:30 a.m. to 7:00 p.m. Monday through Thursday. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Benzion, can be reached at (703) 308-1119. Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. The Fax number is (703) 746-3172. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Young J. Kim

4/6/03



  
KENNETH R. HORLICK, PH.D  
PRIMARY EXAMINER

4/7/03